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REMARKS

An Office Action, Paper No. 4, issued in this application on March 1, 2001. Claims 1-10 are pending and stand rejected. Claims 1-3, 7 and 9 are cancelled herein, claims 4-6, 8, and 10 are amended, and new claims 13-31 are added. Upon entry of this amendment, claims 4-6, 8, 10, and 13-31 remain pending for the Examiner's consideration. The amendments made herein are made generally for the purpose of clarifying the claims over the cited art. Any amendments which are made that limit the scope of claims in any way are done so without prejudice. In addition, the Specification has been amended to correct obvious typographical errors. No new matter has been added by this Amendment.

Rejections under Obviousness-Type Double Patenting

Claims 1-3, 7 and 9 are rejected under the judicially created doctrine of double patenting as being unpatentable over claims 1-25 and 1-31 of U.S. Patent No. 5,925,319 and 5,951,951, respectively. Claims 1-3, 7 and 9 have been canceled herein, thereby obviating this double patenting rejection.

Claims 4-6 and 8 are rejected under the judicially created doctrine of double patenting as being unpatentable over claims 1-40 of U.S. Patent No. 5,972,712. The Examiner states that although the conflicting claims are not identical, they are not patentably distinct from each other because both teach method of evaluating the clotting characteristics of blood. A Terminal Disclaimer with respect to U.S. Patent No. 5,972,712 will be filed when patentable subject matter has been determined.

Rejection under 35 U.S.C. §§ 102(b) and 102(e)

Claims 1, 3, 4 and 6-10 are rejected under 35 U.S.C. §102(b) as being anticipated by Ryan (U.S. Patent No. 4,788,139), Baugh et al. (U.S. Patent No. 4,871,677) or Baugh (U.S. Patent No. 5,314,826) and under 35 U.S.C. §102(e) as being anticipated by Bull et al. (U.S. Patent No. 5,716,796). This rejection is respectfully traversed.

The CAFC has stated that anticipation requires the presence in a single prior art reference of the disclosure of each and every element of the claimed invention, arranged as in the claim. *Lindemann Maschinenefabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1458

(Fed. Cir. 1984); *Altco Standard Corporation v. Tennessee Valley Authority*, 1 USPQ 1337, 1341 (Fed. Cir. 1986); 774 F.2d 1082 (Fed. Cir. 1985). Moreover, to anticipate, a reference must also enable. *In re Schoenwald*, 22 USPQ2d 1671, 1672 (Fed. Cir. 1992).

Claims 1, 3, 7 and 9 have been cancelled herein. With respect to claims 4, 6, 8 and 10, it is believed that the cited references do not disclose every element of these claims, and therefore the cited references do not anticipate claims 4, 6, 8 and 10.

First, the Ryan reference does not anticipate claims 4, 6, 8 and 10 as asserted by the Examiner, nor does the Ryan reference anticipate new claims 13-31. Independent claims 4 and 8 as been amended herein specifically recite that a **sufficient amount of clotting reagent** is added to each sample to **promote clotting**. In contrast, there is absolutely no teaching or suggestion in the Ryan reference to add a sufficient amount of a clotting reagent to the sample to promote clotting, as required by each of the claims of the present invention. Further, there is no teaching or suggestion in the Ryan reference to use different amounts of a platelet activating reagent to determine the platelet functionality or clotting characteristics of a blood sample, as additionally required by the claims of the present invention.

Unlike the claims of the present invention which **require** that clotting occur, the Ryan reference relates to a method of determining platelet aggregation in which clotting is **avoided**. As stated in column 4, lines 19-25 of the Ryan reference, blood is typically collected in potassium EDTA. However, platelets become inactive in EDTA-anticoagulated blood, and consequently their function cannot be measured in these solutions. The purpose of the Ryan invention was to resolve this problem and to develop a method for measuring platelet aggregation that uses a standard platelet counter. Ryan discovered that by adding calcium and citrate ions to an EDTA-anticoagulated blood sample, the inactivating effect of EDTA on platelet function could be reversed. See column 4, lines 52-55. Ryan also discovered that the calcium concentration must fall within a certain range of concentrations. As stated in column 5, lines 6-18 of the Ryan reference, "if excess calcium is added and the sample is allowed to sit for approximately ten minutes before conducting the test, clotting is observed. . . . Clearly, when clotting occurs it is not possible to measure platelet aggregation (see Example 2). Thus, sodium citrate is added to the sample to **avoid clotting**." (Emphasis added). Thus, not only does Ryan not teach the use of a clotting reagent, as required by each of the claims of the present invention, the Ryan reference explicitly teaches away from including a clotting reagent in the reagent

container. Such a reagent would promote clotting, in direct contravention of the teachings of the cited reference.

In summary, the method taught by Ryan must avoid clotting in order to measure platelet functionality, while the method of the present invention requires clotting in order to measure platelet functionality. Further, the method of the present invention requires that each of the aliquot samples contain differing amounts of the platelet activation reagent, which is not taught by the Ryan reference.

For the reasons set out above, the Ryan reference fails to show several elements of claim 4. Consequently, the Ryan reference does not anticipate claim 4. Because the Ryan reference teaches away from the elements of claim 4, the reference, standing alone or in combination with the other cited references, fails to make obvious these elements of claim 4. For at least these reasons, claim 4 is not anticipated or made obvious by the Ryan reference. Claims 6, 8 and 10 depend from claim 4 and therefore include all the novel and non-obvious features of claim 4. Thus for the same reasons, claims 6, 8 and 10 are also novel and non-obvious in view of the Ryan reference. Finally, new claims 13-31 contain similar claim limitations discussed above with respect to claims 4, 6, 8 and 10. For the same reasons, the Ryan reference does not anticipate new claims 13-31. Withdrawal of this Section 102(b) rejection over the Ryan reference is respectfully requested.

Next, the Baugh et al. reference (U.S. Patent No. 4,871,677) also does not anticipate claims 4, 6, 8 and 10 as asserted by the Examiner, nor does the Baugh et al. reference anticipate new claims 13-31. As discussed above, claims 4, 6, 8 and 10 specifically recite adding a sufficient amount of a clotting reagent to the sample to promote clotting. In addition, the claims of the present invention also require adding a platelet activating reagent into each of several aliquots of the blood sample, wherein the amount of platelet activating reagent in each aliquot differs from the amount in the other aliquots. These elements are neither taught nor suggested by the Baugh et al. reference.

The Baugh et al. reference does not state how the blood samples are activated to promote clotting in the activated clotting time test, and more importantly the Baugh et al. reference does not teach adding a sufficient amount of a clotting reagent to the sample to promote clotting, as required in all of the claims of the present invention. Rather, the Baugh et al. reference teaches a

method of analyzing a blood sample which includes adding a platelet **inhibitor** to the blood sample simultaneously with collection of the sample, wherein the inhibitor is effective in inhibiting platelet-related procoagulant activity. As discussed in the Baugh et al. reference, blood samples are typically drawn into a tube containing a calcium chelating agent such as citric acid to prevent the initiating of clotting reactions. However, Baugh et al. discovered that a marked difference in clotting times occurs between an activated clotting time test run at bedside and a test on a citrated blood sample run more than an hour after drawing the sample. See column 3, lines 56-61. To avoid this situation, Baugh et al. taught to include an inhibitor in the citrated collection medium into which the fresh drawn blood sample is collected. See column 6, lines 37-43. This is in direct contrast to the claims of the present invention which require the addition of a sufficient amount of clotting reagent to promote clotting.

Further, the method of the Baugh et al. reference does not include adding a platelet activating reagent into each of several aliquots of the blood sample, wherein the amount of platelet activating reagent in each aliquot differs from the amount in the other aliquots, as specifically required by all of the claims of the present invention.

In summary, the Baugh et al. reference does not teach several elements of the claims of the present invention. First, the Baugh et al. reference does not teach adding a clotting reagent to the sample, let alone sufficient amount a clotting reagent to promote clotting. In addition, the Baugh et al. reference does not teach determining the platelet functionality or clotting characteristics of the blood sample by measuring a change in viscosity of the blood samples. Finally, the Baugh et al. does not teach adding a platelet activating reagent to the blood sample.

For the reasons set out above, the Baugh et al. reference fails to show several elements of claim 4. Consequently, the Baugh et al. reference does not anticipate claim 4. Because the Baugh et al. reference teaches away from the elements of claim 4, the reference, standing alone or in combination with the other cited references, fails to make obvious these elements of claim 4. For at least these reasons, claim 4 is not anticipated or made obvious by the Baugh et al. reference. Claims 6, 8 and 10 depend from claim 4 and therefore include all the novel and non-obvious features of claim 4. Thus for the same reasons, claims 6, 8 and 10 are also novel and non-obvious in view of the Baugh et al. reference. Finally, new claims 13-31 contain similar claim limitations discussed above with respect to claims 4, 6, 8 and 10. For the same reasons, the Baugh et al. reference does not anticipate new claims 13-31. Withdrawal of this Section

102(b) rejection over the Baugh et al. reference is respectfully requested.

Next, the Baugh reference (U.S. Patent No. 5,314,826) also does not anticipate claims 4, 6, 8 and 10 as asserted by the Examiner, nor does the Baugh reference anticipate new claims 13-31.

The present invention provides methods of determining platelet functionality and clotting characteristics of a blood sample by dividing the sample into aliquots adding a platelet activating agent to each of the aliquots, wherein the aliquots each contain differing amounts of the platelet activating reagent. The platelet activating reagent enhances the ability of active platelets to effectively participate in the blood clotting reaction and thereby shorten the clotting time of the blood. If the platelets are inactive or not functioning normally, the activating reagent will have a lessened or no effect on the clotting time.

In contrast, the Baugh reference relates to an improved activated clotting time (ACT) test which accommodates the effects of platelet activation by incorporating a platelet activation phase. Baugh discovered that the initial contact and interaction of the blood sample with the activating reagent affects the platelet activation, which may make the ACT test results variable and operator dependent. In one embodiment, Baugh provides a two-phase ACT test which accommodates the rate at which platelet activation contributes to an ACT by controlling the activation in a specific platelet activation phase of the test. Following this phase, the ACT test continues through a typical clotting test phase. The Baugh reference also describes a platelet functionality test which uses two simultaneous ACT tests, one with a platelet activation phase which normally achieves a relatively high rate of contribution from platelet activation to clotting, and the other with a platelet activation phase which normally achieves a relatively lower rate of contribution from platelet activation to clotting. The difference between the clotting times of the two ACT tests is indicative of the platelet functionality of the sample of blood. Both of the tests described in the Baugh reference involve mixing the blood sample with a activating agent, for example an activating surface reagent such as kaolin. However, there is absolutely no teaching or suggestion in the Baugh reference to include a chemical platelet activating reagent or a clotting affecting reagent in the test cells, let alone to use different amounts of the platelet activating reagent to determine the platelet functionality or the clotting characteristics of the blood sample, as required by the claims of the present invention.

For the reasons set out above, the Baugh reference fails to show every elements of claim 4. Consequently, the Baugh reference does not anticipate claim 4. Because the Baugh reference teaches away from the elements of claim 4, the reference, standing alone or in combination with the other cited references, fails to make obvious these elements of claim 4. For at least these reasons, claim 4 is not anticipated or made obvious by the Baugh reference. Claims 6, 8 and 10 depend from claim 4 and therefore include all the novel and non-obvious features of claim 4. Thus for the same reasons, claims 6, 8 and 10 are also novel and non-obvious in view of the Baugh reference. Finally, new claims 13-31 contain similar claim limitations discussed above with respect to claims 4, 6, 8 and 10. For the same reasons, the Baugh reference does not anticipate new claims 13-31. Withdrawal of this Section 102(b) rejection over the Baugh reference is respectfully requested.

Finally, the Bull et al. reference (U.S. Patent No. 5,716,796) also does not anticipate claims 4, 6, 8 and 10 as asserted by the Examiner, nor does the Bull et al. reference anticipate new claims 13-31.

Claim 4 as amended herein is directed to a method of determining platelet functionality of a blood sample, comprising dividing the blood sample into aliquots and:

> adding a predetermined amount of a platelet activating reagent to each of said aliquot samples, the amount of said platelet activating reagent in each said aliquot sample differing from the amount of said platelet activating reagent in each other aliquot sample;
>
> adding a **sufficient amount of a clotting reagent** to each said aliquot sample **to promote clotting**;
>
> performing a clotting test on each said aliquot sample; and
>
> determining said platelet functionality of said sample based on the difference in clotting times for each said aliquot sample, **wherein said clotting times are determined by measuring a change in viscosity of said aliquot samples**.

The Bull et al. reference differs from the invention of claim 4 in several critical aspects. The Bull et al. reference teaches a method for detecting platelet aggregation which involves forming a mixture of a disclosure reagent (e.g., diatomaceous earth) which adheres to platelets, and a platelet agonist which activates platelets and initiates platelet clumping. This mixture is

added to the blood sample and platelet aggregation is detected by visualizing platelet clumping without contacting the blood sample with a foreign measuring object. The purpose of the Bull et al. reference was to overcome timing issues in evaluating platelet functional activity. That is, intent of the Bull et al. method is to **delay the onset of clotting** in order to make the platelet aggregation visible to measurement. This procedure was necessary, since the optical detection method used by Bull et al. is unable to discriminate between platelet aggregation and clot formation. Therefore, the method of Bull et al. for determining platelet aggregation involves a **small amount** of a matrix for platelet clumping (e.g., diatomaceous earth) to activate platelets and provide a matrix for platelet clumping, but which does **not** result in clot formation. See column 4, lines 43-53 and column 7, lines 4-5. This is in direct contrast to the method of the present invention, which specifically requires a sufficient amount of a clotting reagent to **promote clotting**.

Secondly, the method of Bull et al. further requires that the specimen be contained in a tube that is held in a nearly horizontal position that is capable of both rotating and rocking, thus producing a thin layer of whole blood on the inner wall of the specimen container, such that the layer is sufficiently transparent to permit **optical end-point detection**. See column 4, lines 53-57 and column 5, lines 34-37. In the method of Bull et al., the diatomaceous earth causes the platelets to form clumps which become sticky and adhere to the wall of the container during rotation and rocking of the container. In contrast, the method of the present invention **requires** clot formation to determine platelet functionality, and measures the clot formation by measuring a **change in viscosity** of the sample.

In summary, since the Bull et al. reference teaches away from clot formation in evaluating platelet functionality, and teaches detection of platelet aggregation by optical end-point detection of platelet-diatomaceous earth clumps, the Bull et al. reference does not teach every element of claim 4. For at least these reasons, the Bull et al. reference fails to show every elements of claim 4. Consequently, the Bull et al. reference does not anticipate claim 4. Because the Bull et al. reference teaches away from the elements of claim 4, the reference, standing alone or in combination with the other cited references, fails to make obvious these elements of claim 4. For at least these reasons, claim 4 is not anticipated or made obvious by the Bull et al. reference. Claims 6, 8 and 10 depend from claim 4 and therefore include all the novel and non-obvious features of claim 4. Thus for the same reasons, claims 6, 8 and 10 are also

novel and non-obvious in view of the Bull et al. reference. Finally, new claims 13-31 contain similar claim limitations discussed above with respect to claims 4, 6, 8 and 10. For the same reasons, the Bull et al. reference does not anticipate new claims 13-31. Withdrawal of this Section 102(e) rejection over the Bull et al. reference is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 2 and 5 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ryan (4,788,139), Baugh et al. (4,871,677), Baugh (5,314,826) or Bull et al. (5,716,796) in view of Hanahan et al. (4.329,302). The Examiner states that the cited art teaches methods and apparatus for the evaluation of clotting characteristics of platelets. The Examiner also states that while the art is silent to the claimed 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine, the Hanahan et al. references teaches 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine is a potent platelet activator. The Examiner then concludes that is would have been within the skill of the art to modify Ryan, Baugh et al., Baugh or Bull in view of Hanahan et al. and use 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine to gain the advantage of high platelet activation. This rejection is respectfully traversed.

As discussed above in detail, none of the cited art, alone or in combination, teaches or suggests the method of the present invention. Claim 2 has been cancelled herein, and claim 5 depends indirectly from claim 4, which as discussed above is novel and non-obvious in view of the prior art. Since claim 5 includes all the claim limitations of claim 4, claim 4 is also novel and non-obvious in view of the cited art for the same reasons discussed above with respect to claim 4.

Briefly, as discussed above, modifying the method of Ryan by including a sufficient amount of a clotting reagent to promote clotting would destroy the intended function of the cited reference. Specifically, as mentioned above, such a reagent would promote clotting and thus prevent the completion of Ryan's platelet aggregation test. Thus, while the method of the present invention measures the platelet functionality and clotting characteristics of a blood sample based on the ability of the blood to clot, the Ryan reference specifically teaches to "avoid clotting," since "when clotting occurs it is not possible to measure platelet aggregation," which is the purpose of the Ryan invention. A Section 103 rejection based upon a modification of a reference that destroys the intent, purpose or function of the invention disclosed in the reference

is not proper, and a *prima facie* case of obviousness cannot be properly made. In short, there would be no technological motivation for engaging in the modification or change. To the contrary, there would be a disincentive. *In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984).

Further, the fact that Hanahan et al. teach 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine as a platelet activator is irrelevant to the patentability of the present invention, since the combination of the Ryan reference with the Hanahan et al. reference still would not teach or suggest the method of the present invention. In fact, Ryan does indeed teach adding a platelet aggregating reagent, however, the goal of Ryan is to avoid clotting, and therefore the addition of a platelet aggregating reagent to the method of Ryan does not teach or suggest the method of the present invention.

Next, the Baugh et al. reference does not teach adding a sufficient amount of a clotting reagent to the sample to promote clotting, as required in all of the claims of the present invention. Further, the method of the Baugh et al. reference does not include adding a platelet activating reagent into each of several aliquots of the blood sample, wherein the amount of platelet activating reagent in each aliquot differs from the amount in the other aliquots, as specifically required by all of the claims of the present invention. As such, the Baugh et al. reference does not render the method of the present invention obvious.

Further, the fact that Hanahan et al. teach 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine as a platelet activator is irrelevant to the patentability of the present invention, since the Baugh et al. reference provides no motivation to one skilled in the art to modify the method of Baugh et al. by adding a platelet activator.

Next, the Baugh reference does not teach or suggest adding a chemical platelet activating reagent or a clotting affecting reagent in the test cells, let alone to use different amounts of the platelet activating reagent to determine the platelet functionality or the clotting characteristics of the blood sample, as required by the claims of the present invention. Without some suggestion in the cited art, there is no incentive for one of skill in the art to modify the method of the Baugh reference by adding a chemical platelet activating agent. As such, the Baugh reference does not render the method of the present invention obvious.

Further, the fact that Hanahan et al. teach 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine as a platelet activator is irrelevant to the patentability of the present invention, since the Baugh reference provides no motivation to one skilled in the art to modify the method

of Baugh by adding a platelet activator.

Finally, as discussed above, the Bull et al. reference specifically teaches away from clot formation in their method of evaluating platelet functionality. Thus, while the method of the present invention measures the platelet functionality and clotting characteristics of a blood sample based on the ability of the blood to **clot**, the Bull et al. reference specifically teaches to "delay the onset of clotting," since when clotting occurs it is not possible to measure platelet aggregation, which is the purpose of the Bull et al. invention. A Section 103 rejection based upon a modification of a reference that destroys the intent, purpose or function of the invention disclosed in the reference is not proper, and a *prima facie* case of obviousness cannot be properly made.

Further, the fact that Hanahan et al. teach 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine as a platelet activator is irrelevant to the patentability of the present invention, since the combination of the Bull et al. reference with the Hanahan et al. reference still would not teach or suggest the method of the present invention. The goal of Bull et al. is to avoid clotting, and therefore, even if there were a suggestion in the Bull et al. reference to add a platelet aggregating reagent (which there is not), the modification still would not teach or suggest the method of the present invention.

For the reasons stated above, the combination of the Ryan, Baugh et al., Baugh or Bull et al. reference with the Hanahan et al. reference does not teach or suggest the method of the present invention. Withdrawal of the Section 103(a) rejection of claims 2 and 5 over Ryan, Baugh et al., Baugh or Bull et al. in view of Hanahan et al. is respectfully requested.

CONCLUSIONS

It is believed that all the claims now pending in this patent application, as amended and described above, are now allowable. Therefore, it is respectfully requested that the Examiner reconsider his rejections and to grant an early allowance. If any questions or issues remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number listed below.

It is believed that no fees are required in filing this Amendment and Remarks. However, should any fee be required, please charge Deposit Account No. 50-1123.

Respectfully submitted,

May 29, 2001
Dated

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VERSION WITH MARKING SHOWING CHANGES MADE TO SPECIFICATION

Please amend the paragraph starting on page 2, line 27 as follows:

In accordance with the foregoing objects, the present invention is embodied in a cartridge having a plurality of test cells. Each cell is adapted for receiving an aliquot part of a blood sample. A measured amount of [clotting] platelet activating reagent is applied in the reaction chamber of each cell as a dried fill. The amount of reagent in each cell differs from the amount of reagent in each other cell, at least one of the cells containing no platelet activating reagent. Additionally, amounts of heparin or protamine may be added in each cell either as a liquid or a dried fill. The cells also include a clotting reagent such as kaolin which on use of the cartridge is inserted into the reaction chamber and mixed with the blood and platelet [activation] activating reagent. The relative clotting times of the samples in each of the cells [is] are measured and, when compared to a standard and each other, [determines] determine the platelet functionality of the blood sample.

Please amend the paragraph starting on page 3, line 25 as follows:

The present invention is embodied in a test cartridge 10 having a plurality of test cells 11, preferably six such cells, depending from and integral with a cartridge plate 12 having a front depending skirt or panel 14. The cartridge is adapted to be inserted into a test apparatus such as shown and described in detail in U.S. Pat. No. 4,599,219 for the determination of THE clotting time of an aliquot blood sample inserted into each test cell 11 as described in detail in said patent. Each cell is formed by a downwardly tapered tube 15 defining an inwardly projecting annular seat 16 intermediate its ends and in turn defining an upper sealing surface 18 and a lower sealing surface 19. A resilient flexible sliding plug 20 is positioned in the lower end of the tube 15 while a plunger 21 defined by a plunger shaft 22 and a sealing washer or disk 24 is positioned in the upper portion of the tube. The sealing washer 24 seats against the upper sealing surface 18 of the annular seat and defines with the plug 20 a lower clotting reagent chamber 25. The tube 15 defines above the washer 24 [a blood receiving] an upper cell reaction chamber 26. At its upper end the plunger 21 defines a flag 28 and is adapted for engagement by the test machine (not shown).

Please amend the paragraph starting on line 23 of page 4 as follows:

In accordance with the present invention, a measured amount of a chemical platelet activating factor or reagent 30 is provided in the top or upper reaction chamber 26 as a dried fill. This platelet activating factor composition is dissolved in the blood sample when the blood sample is introduced into the [clotting] upper reaction chamber 26 and the clotting reagent 29 added and mixed therein. Additionally, selected amounts of heparin or protamine may be utilized as a dried fill in the upper reaction chamber 26, depending on the chemical procedure to be utilized.

Please amend the paragraph starting on line 8 of page 6 as follows:

After introducing the blood samples in each [cell] upper reaction chamber 26, the clotting reagent is inserted into each upper reaction chamber and the clotting time of the blood in each cell is determined. From the clotting time for each cell, the clot ratio is calculated. Clot ratio is the ratio of the clotting times for cells C, D, E and F compared to the average control clotting times[, Cells 11A and 11B] for cells A and B. Platelet function is expressed as a percentage of the maximum clot ratio response observed in a normal population. This value of a normal population response is known and can be used to compute the clot ratio percentage which is in turn indicative of the platelet functionality. Any appropriate desired calculation may be made from the relative clotting times in each cell. The platelet functionality can in turn [by] be utilized to determine blood loss during surgery and the need for a blood transfusion. The platelet functionality further assists in managing heparin therapy during cardiac surgery.

MARKED UP VERSION SHOWING CHANGES MADE TO CLAIMS

Please cancel claims 1-3, 7 and 9.

Please amend claims 4-6, 8 and 10 as follow:

4. (Amended) A method for determining platelet functionality [in] of a blood sample, the method comprising:

(a) dividing said sample into a plurality of aliquot samples[,];

(b) adding a selected amount of a platelet activating reagent to each of said aliquot samples, the amount of said platelet activating reagent in each said aliquot sample differing from the amount of said platelet activating reagent in each other aliquot sample;

(c) adding a sufficient amount of a clotting reagent to each said aliquot sample to promote clotting;

(d) performing a clotting test on each said aliquot sample; [in the presence of a selected amount of a platelet activation reagent, the selected amount of platelet activation reagent for each aliquot sample being different one from another,] and

(e) determining said platelet functionality of said sample based on the difference in clotting times for each said aliquot sample, wherein said clotting times are determined by measuring a change in viscosity of said aliquot samples.

5. (Amended) [A] The method [as defined in] of claim [4] 6, wherein said platelet [activation] activating reagent is 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine.

6. (Amended) [A] The method [as defined in] of claim 4, wherein said platelet [activation] activating reagent is selected from the group consisting of 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine, collagen, epinephrine, ristocetin and arachidonic acid.

8. (Amended) A method for determining clotting characteristics of a blood sample, said method comprising:

(a) dividing said sample into a plurality of aliquot samples[,];

(b) adding a selected amount of a clotting affecting reagent to each said aliquot sample, the amount of clotting affecting reagent in each said sample differing from the amount in each other aliquot sample;

(c) adding a sufficient amount of a clotting reagent to each said sample to promote clotting;

(d) performing a clotting test on each said aliquot sample; [in the presence of a selected amount of a clotting affecting reagent, the selected amount of reagent for each aliquot sample being different one from another,] and

(e) determining clotting characteristics of said sample based on the difference in clotting times for each said aliquot sample.

10. (Amended) [A] The method [as defined in] of claim 8, wherein said clotting affecting reagent is a platelet [activator] activating reagent.

Please add the following new claims 13-31:

13. (New) The method of claim 4, wherein the amount of said platelet activating agent in each said aliquot sample is between about 0 and about 2.76 micrograms.

14. (New) The method of claim 4, wherein the concentration of said platelet activating reagent in each said aliquot sample is between about 0 and about 150 nM.

15. (New) The method of claim 4, wherein at least one of said aliquot samples contains no platelet activating reagent and each remaining aliquot sample comprises different amounts of said platelet activating reagent.

16. (New) The method of claim 4, wherein said clotting reagent is kaolin.

17. (New) The method of claim 4, wherein the change in viscosity is determined using a plunger sensor technique.

18. (New) The method of claim 10, wherein said platelet activating reagent is selected from the group consisting of 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine, collagen, epinephrine, ristocetin and arachidonic acid.

19. (New) The method of claim 18, wherein said platelet activating reagent is 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine.

20. (New) The method of claim 10, wherein the amount of said platelet activating agent in each said aliquot sample is between about 0 and about 2.76 micrograms.

21. (New) The method of claim 10, wherein the concentration of said platelet activating reagent in each said aliquot sample is between about 0 and about 150 nM.

22. (New) The method of claim 8, wherein at least one of said aliquot samples contains no platelet activating reagent, and wherein each remaining aliquot sample comprises

different amounts of said platelet activating reagent.

23. (New) The method of claim 8, wherein said clotting reagent is kaolin.

24. (New) The method of claim 8, wherein said clotting times are determined by measuring a change in viscosity of each of said aliquot samples.

25. (New) The method of claim 24, wherein said change in viscosity is measured by a plunger sensor technique.

26. (New) A method for performing an activated clotting time test on a sample of blood using a multicell test cartridge, said cartridge comprising at least a first, a second and a third test cell, each of said cells comprising a sufficient amount of a contact activator to achieve clotting, wherein said first cell further comprises a first amount of a platelet activating reagent and wherein said second cell comprises a second amount of said platelet activating reagent, said first and second amounts being different, said method comprising:

(a) dividing said sample into first, second and third partial samples;

(b) dispensing the first partial sample into the first test cell to form a first test mixture;

(c) performing a first activated clotting time test on the first test mixture to obtain a first clotting time;

(d) repeating the aforementioned steps of dispensing and performing an activated clotting time test on each of said second and third partial samples to obtain a second and third clotting time; and

(e) comparing the clotting time of said first, second, and third partial samples to determine the activated clotting time of the sample of blood based on the clotting time times of said first, second and third partial samples.

27. (New) The method of claim 26, wherein said platelet activating reagent is selected from the group consisting of 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine, collagen, epinephrine, ristocetin and arachidonic acid.

28. (New) The method of claim 26, wherein said platelet activating reagent is 1-O-alkyl-2-acetyl-sn-glyceryl-3-phosphorylcholine.

29. (New) The method of claim 26, wherein said clotting reagent is kaolin.

30. (New) The method of claim 26, wherein said clotting times are determined by measuring a change in viscosity of each of said aliquot samples.

31. (New) The method of claim 30, wherein said change in viscosity is measured by a plunger sensor technique.